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Original Article

Sleep variability and cardiac autonomic modulation in adolescents – Penn State Child Cohort (PSCC) study

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ABSTRACT

Objective: To investigate the effects of objectively measured habitual sleep patterns on cardiac autonomic modulation (CAM) in a population-based sample of adolescents.
Methods: We used data from 421 adolescents who completed the follow-up examination in the Penn State Children Cohort study. CAM was assessed by heart rate (HR) variability (HRV) analysis of beat-to-beat normal R-R intervals from a 39-h electrocardiogram, on a 30-min basis. The HRV indices included frequency domain (HF, LF, and LF/HF ratio), and time domain (SDNN, RMSSD, and heart rate or HR) variables. Actigraphy was used for seven consecutive nights to estimate nightly sleep duration and time in bed. The seven-night mean (SD) of sleep duration and sleep efficiency were used to represent sleep duration, duration variability, sleep efficiency, and efficiency variability, respectively. HF and LF were log-transformed for statistical analysis. Linear mixed-effect models were used to analyze the association between sleep patterns and CAM.
Results: After adjusting for major confounders, increased sleep duration variability and efficiency variability were significantly associated with lower HRV and higher HR during the 39-h, as well as separated by daytime and nighttime. For instance, a 1-h increase in sleep duration variability is associated with –0.14(0.04), –0.12(0.06), and –0.16(0.05) ms^2 decrease in total, daytime, and nighttime HF, respectively. No associations were found between sleep duration, or sleep efficiency and HRV.
Conclusion: Higher habitual sleep duration variability and efficiency variability are associated with lower HRV and higher HR, suggesting that an irregular sleep pattern has an adverse impact on CAM, even in healthy adolescents.

1. Introduction

Due to the modern, around-the-clock lifestyles, many people form poor habitual sleep patterns and experience sleep disturbances and sleep deprivation. A number of epidemiological studies have demonstrated that sleep disturbance and short sleep duration are associated with adverse cardiovascular outcomes, such as hypertension, diabetes, and obesity [1–6]. Additionally, a recently published meta-analysis in adults demonstrated that short sleep duration was associated with increased risk of coronary heart disease mortality [7]. Not only is short sleep duration common among adults, but it is also a growing problem even among children and adolescents [8–10]. Recent studies have reported that, on average, adolescents sleep <8 h per night, which is less than the recommended 9 h of sleep [11–14]. More importantly, short sleep duration has been associated with disrupted autonomic nervous system function, a predictor of cardiovascular diseases (CVDs), in children [15,16]. As children and adolescents are in a developmental period and at a critical time of forming sleep habits, they may benefit by acquiring the habit of getting enough sleep and consequently reduce CVD risk in adulthood. However, the vast majority of the previous studies were based on subjectively reported sleep duration instead of objectively measured sleep duration. As subjectively

Abbreviations: BMI, Body mass index; CAM, Cardiac autonomic modulation; CVD, Cardiovascular diseases; EGC, Electrocardiography; HF, High-frequency range; HR, Heart rate; HRV, Heart rate variability; LF, Left frequency range; LF/HF, The ratio of LF to HF; PSCC, Penn State Children Cohort; PSG, Polysomnography; RMSSD, Square root of the mean of the sum of the squares of differences between adjacent RR intervals; SD, Standard deviation; SDNN, Standard deviation of all RR intervals.

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measured sleep duration is weakly correlated with objective sleep duration, one can argue that subjectively measured sleep duration may serve as a surrogate of stress, anxiety, and depression. Thus, the association between subjectively measured short sleep duration may be biased by psychological conditions of the participants.

On the other hand, with increased availability of noninvasive methods of monitoring multiple nights of sleep, like actigraphy, objectively measured habitual sleep patterns, such as the variability in sleep duration or sleep efficiency (the percentage of actual sleep duration during the total time in bed), have been utilized in sleep studies [17–21]. Although there is very little direct evidence linking habitual sleep patterns and CVD risk, it has been associated with CVD risk factors, such as insomnia [19,22,23]. Specifically, if someone does not sleep enough on one night, then that person may try to sleep longer the next night in an attempt to "recover" the sleep that was lost. Although the so-called "recovery" sleep may provide some temporary improvement, it could also result in less total sleep time or lower sleep efficiency on subsequent nights, as too much "recovery" sleep may paradoxically impair the ability to fall asleep on the next night [23,24]. More important, our group has reported an association between insomnia symptoms and impaired heart rate variability (HRV) in children [22]. Therefore, it is plausible that high variability in habitual sleep pattern may lead to impaired cardiac autonomic modulation (CAM).

Heart rate variability HRV is commonly used as a noninvasive measurement of CAM [25], and is regulated by the balance of sympathetic and parasympathetic modulation. Lower HRV calculated from short-term normal RR intervals, ranging from minutes to hours has been associated with CVD mortality and morbidity in various populations [26–32]. The associations between habitual sleep patterns and CAM in adolescents have not been fully understood. In recent years, only two epidemiological studies have reported association between short sleep duration and cardiac autonomic dysfunction in children [15,16]. However, these studies only examined the effect of mean sleep duration, but not the variability, on CAM. Thus, the objective of this study is to investigate, in a population-based-sample of adolescents, the association between objectively measured habitual sleep patterns (mean sleep duration, sleep duration variability, mean sleep efficiency, and sleep efficiency variability) and CAM.

2. Methods

2.1. Study population

We used available data from 421 adolescents who completed the follow-up examination of the Penn State Children Cohort (PSCC) study. The recruitment and examination procedures for the baseline study have been published elsewhere [18]. During 2010–2013, a follow-up examination was conducted. Among the 700 baseline study participants, 421 of them completed the follow-up examination, with a response rate of 60% and a mean (standard deviation or SD) follow-up time of 7.7 (1.4) years. The loss to follow-up was mainly due to subjects moving out of central Pennsylvania. However, no major difference in baseline characteristics was observed between subjects who did and did not participate. During the study period, participants were evaluated overnight in the Clinical Research Center at the Pennsylvania State University College of Medicine including a complete physical examination, a whole body dual-energy X-ray absorptiometry, and a 9-h fixed-time polysomnography (PSG) recording. Blood, saliva, and urine samples were collected after the overnight fasting. After being released from the overnight stay, they were given a set of questionnaires about habitual behavior, and an activity log. A high-fidelity Holter electrocardiogram (ECG) monitor was used to record beat-to-beat ECG during the overnight stay and 24 h after the participant was released, resulting in a total of 39 h recording.

To collect objective night-to-night sleep data, participants wore an actigraph tri-axis accelerometer monitor (GT3X+, Actigraph LLC, Pensacola, FL, USA) for eight consecutive nights (including the night at the sleep laboratory during the PSG) on their wrist of the nondominant hand during bedtime, in conjunction with a sleep diary that recorded "bed time" and "out of bed time" on nightly basis. The actigraphy data were exported to a designated computer for analysis. After an experienced investigator removed the artifacts from the actigraphy data, the total sleep time in bed and the actual sleep duration were obtained by using ActLife 6 software (Actigraph LLC, Pensacola, FL, USA). Sleep data for the first night were excluded from the analysis, as they were measured in a controlled setting under a 9-h fixed sleep protocol. Thus, seven consecutive nights of sleep data were used in this report. The study protocol was approved by Pennsylvania State University College of Medicine IRB. Written informed consent was obtained from participants and their parents if participant was a minor (<18 years old).

2.2. Sleep variables

We objectively assessed the habitual sleep pattern for each participant by using seven-night actigraphy data. After carefully examining and removing any artifacts from the actigraphy data, the following sleep parameters were directly calculated for each night: (1) total in bed time; (2) the total sleep time; and (3) sleep efficiency, which is the percentage of actual sleep duration during the total time in bed [(Sleep duration/Time in bed)*100%]. Based on the total sleep time and sleep efficiency in seven consecutive nights, we calculated the following variables to represent the participants' habitual sleep pattern: (1) the mean of total sleep time as habitual sleep duration; (2) the SD of the mean sleep duration as habitual sleep duration variability; (3) the mean of sleep efficiency as habitual sleep efficiency; and (4) the SD of the mean sleep efficiency as the habitual sleep efficiency variability. Participants with less than five (<5) nights, that is, less than 70% of seven nights, of sleep data were excluded from this report.

2.3. Continuous Holter ECG recording

A high-fidelity (sampling frequency 1000 Hz) 12-lead HScribe Holter System (Mortara Instrument, Inc., Milwaukee, WI, USA) was used to collect the 39-h Holter beat-to-beat ECG data. The high-fidelity ECG significantly increases the resolution and enhances the accuracy of various waveform measurements. All Holter recordings started between 5:00 PM and 7:00 PM. The Holter ECG data were scanned to a designated computer for offline processing by an experienced investigator using specialized SuperECG software (Mortara Instrument, Inc., Milwaukee, WI, USA). The standardized operation procedures for the PSCC study were followed rigorously in the data collection, offline processes, HRV analysis, and interpretation processes. Briefly, the Holter ECG Data Collection and Analysis Procedures were followed to prepare, hook up, calibrate, and start the Holter digital recorder. After 39 h of recording, a trained investigator retrieved and archived the beat-to-beat ECG data for offline processing. The main objective of the offline processing was to verify the Holter-identified ECG waves and to identify and label additional electronic artifacts and arrhythmic beats in the ECG recording. Finally, a single research investigator performed beat-to-beat HRV analysis using the normal beat-to-beat RR interval data.